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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,368	10/26/2001	James P. Hoeffler	INVIT1100-2	2504

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DLA PIPER RUDNICK GRAY CARY US, LLP
4365 EXECUTIVE DRIVE
SUITE 1100
SAN DIEGO, CA 92121-2133

EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,368	HOEFFLER ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,20-24 and 48-70* is/are pending in the application.

4a) Of the above claim(s) *20,51-54 and 56-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18, 21-24, 48-50, 55 and 60-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S02

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 August 2005 has been entered.

Amendment Entry

2. Applicants' response to the final office action mailed 29 December 2004 is acknowledged (Paper filed 8/31/05). In the amendment filed therein claims 18 was modified. Currently claims 18, 21-24, 48-50, 55, and 60-70 are under consideration.

3. Rejections and/or Objections of record not reiterated below have been withdrawn.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 18, 21-24, 48-50, 55 and 60-70 are rejected under 35 U.S.C. 1 12, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The term "uncharacterized" in claims 31 and 37 is a relative term, which renders the claim indefinite. The term "uncharacterized" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree', and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to what applicant intends to encompass with respect to the antibodies (what makes them uncharacterized – unknown binding affinity). Are uncharacterized antibodies directed to any known antibody or unknown antibodies? Are "uncharacterized antibodies" defining the binding ability of the antibody? For example it is not known what antigen binds the antibodies? Or does "uncharacterized" mean the antibodies are to meet some other parameter not clearly identified. It is suggested that the term be removed or defined such that the intended meaning is clear. Please clarify.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 18, 21, 22, 55 and 64-67 are rejected under 35 U.S.C. 103(a) as being obvious over Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070).

Couchman et al. disclose methods to screen for differentially expressed proteins in cDNA libraries (cell lysates). The cDNA libraries were human secretory and proliferative endometrium samples (normal and abnormal endometrium). The cDNA libraries were screened with a polyclonal anti-phosphotyrosine antibody. A differentially expressed protein named Lyn was found to be associated with human endometrial adenocarcinomas (cancer cells). See abstract.

Couchman et al. differ from the instant invention in not specifically teaching an array configuration including uncharacterized antibodies.

However, Kauvar teach method of characterizing drugs (proteins) via antibody arrays comprising different binding affinities. The antibody arrays produce characteristic profiles (protein profiles), which can be evaluated or compared to assess the analyte in compound detected. See abstract and figure 5.

The antibodies used were mostly IgG, IgM forms (uncharacterized anatibodies meeting the limitation of claim 55) with vary binding affinity (binding coefficients). See column 8 line 11-14 and figure 2B.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to employ various immunoglobulin antibodies (IgG and IgM) with various affinities in arrays as taught by Kauvar in the method of Couchman et al. because Kauvar taught that his invention offered a method of profiling a particular analyte by taking advantage of its specific pattern of reactivity against a panel of antibodies of varying specificity and affinity. Column 3 lines 11-24. Further, in this array format small quantities of analyte can be tested against a large collection of potentially cross reactive antibodies to generate rapid, low cost, data analysis. Column 4 lines 60-67.

II. Claims 23, 24, 48-50 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) and further in view of Spencer et al. (WO 93/12248).

Please see Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) as set forth above.

Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) differ from the instant invention in not specifically teaching cell lysate comparison procedures wherein the cell population is modified. In particular, the comparison of normal cells to stimulated cells, single tissue type to different species, and the same tissue at different development stages.

However Spencer et al. disclose the evaluation of binding patterns to identify cell lysates involved in inflammatory conditions. The cell population is modified to test for binding capabilities. See abstract and page 2 line 34 –page 3 line 1. Cell lysates or cell lines labeled for detection are exemplified on page 6 line 36 to page 7 line 13. Page 9 lines 8-22 describe various cell comparisons as recited in the claims. See activated T cell/stimulated (page 9 line 12), fetal cell/developmental stage (page 9 line 20), tonsil and spleen cells/different tissue types (page 14 line 34), resting state (page 14 line 39), mouse-cell line (page 23), human-cell lines (page 19-20). The use of these binding analyses, were taught to be useful in the diagnosis and treatment of inflammatory disease, such as Crohn's disease.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use various cell lysate comparisons as taught by Spencer et al. in the method of Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) because Spencer et al. taught that The use of these binding analyses, were taught to be useful in the diagnosis and treatment of inflammatory disease, such as Crohn's disease. See abstract.

III. Claims 60-63 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) and further in view of James F. Cupo (Journal of Chromatography, 569, 1991, 389-40).

Please see Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) as set forth above.

Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) differ from the instant invention in not teaching protein expression pattern evaluation in virus cell lines (like T cells) and further allowing for cellular replication distinctions (differential development) via polyacrylamide.

However, Cupo teaches a two-dimensional polyacrylamide gel electrophoresis procedure to measure matrix proteins. The proteins are tissue-type specific and can reflect changes in the state of differentiation of a cell.

The method can further distinguish between a diseased cell and a normal cell. The disease states include various cancers, autoimmune disease, and adenoviral infection. See abstract. The method is quick and efficient employing the appropriate antibodies to the protein of interest. Page 403, 1st paragraph. Protein patterning in T lymphocytes (T cells) is outlined on page 400. The method is used to detect early stages of viral infection because a virus must replicate cellular components associated with the nuclear matrix. Such changes are evident in protein patterning analysis. See page 403 – 4.3.

With respect to the solid phase possibilities listed in claims 60-62, it is noted that various solid phase compositions are taught in the prior art. Absent evidence to the contrary the selection of any one of the known solid phase surfaces is routine adjustment of the solid phase methods exhibited by the cited prior art.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use protein patterning procedures to evaluate virus cell lines (like T cells) and further allowing for cellular replication distinctions (differential development) via polyacrylamide as taught by Cupo in the high through put protein pattering procedure of Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) because Cupo taught that two-dimensional gels can determine tissue-type specific differences in nuclear matrix proteins and the differences between normal and carcinogenic cells. See page 402 - 4.2

Further these proteins play an important role in cells. Utilization of the proteins can lead to the development of diagnostic agents to detect various diseased conditions of the cell and organism (including cancer and viruses). Cupo page 404.

IV. Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) and further in view of Ganz et al. (Biochemistry and Cell Biology, 1991, Vol.69, No.7, pages 442-448).

Please see Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) as set forth above.

Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) differ from the instant invention in not specifically teaching the first cell lysate comprising an arterial endothelial cell lysate and the second cell lysate comprising a venous endothelial cell lysate.

However, Ganz et al. disclose that phenotypic and biochemical diversity exists between endothelial cells. Ligand binding experiments with labeled plasminogen were analyzed in arterial, capillary, and venous endothelial cells. This analysis demonstrated that the various endothelial cells exhibited distinct binding difference. See abstract and page 446 Discussion.

Ganz et al. establish that the same cells types (endothelial cells) from different sources (arterial, capillary, and venous) exhibit different binding patterns. See abstract.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ compare various sources of cells as taught by Ganz et al. in the high through put protein pattering procedure of Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) in order to identify different proteins with possibly different characteristics. See page 446 Discussion.

Further modifications with respect to the type of cells evaluated in the instant method are viewed as mere design choice and optimization. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to various cells and sources in the methods of Couchman et al. in view of Kauvar because it would have been an obvious combination of a known cells to evaluate their protein expression via the methods taught by Couchman et al. in view of Kauvar.

The changes in cell type for evaluation are routine optimizations that are almost always determined and used in methods to test the properties of interest.

Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to analyze various cell types in the given parameters to determine the unknown as a means of optimizing the methods provided by the art.

Response to Arguments

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant arguments against Baecher-Allen et al., Ekins et al., and Yates et al. are MOOT because the references have been withdrawn. The combination of Couchman et al. (Journal of the Society for Gynecologic Investigation, 1997, 4(2), 103-109 Abstract Only) in view of Kauvar (US Patent #5,541,070) have been cited to make the instant invention obvious.

With respect to the rejections under 35 USC 103 (a), including Cupo, Applicant contends that the deficiencies of the primary references (Yates with Baecher-Allen et al. and Elkins et a.) are not overcome by the addition of the references to Cupo or Kauvar. This argument was carefully considered but not found persuasive because the primary references have been addressed above.

With respect to the rejection over claim 68, Applicant contends that examiner should provide a reference demonstrating obviousness. According the reference to Ganz et al. has been added to the rejections.

5. For reasons aforementioned, no claims are allowed.

Remarks

6. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Stevenson et al. (Biomarkers, 1997, 2, 63-65) disclose ELISA procedures (arrays) involving uncharacterized antibodies. See abstract and page 63 2nd column, 2nd paragraph. Specifically, uncharacterized antibodies to collagen IV are shown to be elevated in basement membrane damage. See page 64 - Discussion. The increased serum levels of less characterized (uncharacterized) antibodies may be useful in determining antibody-mediated diseases and basement membrane disturbances. See page 63 1st column last lines through 2nd column lines 7.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lisa V. Cook

Lisa V. Cook
Remsen 3C-59
(571) 272-0816
10/1/05

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
10/03/05